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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,091	02/01/2002	Marshall D. Crew	PC23132A	7361

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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/066,091	MARSHALL D. CREW	
	Examiner	Art Unit	
	Blessing M. Fubara	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ ~~Claim(s) *1-25* is/are pending in the application.~~

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/5/03 & 05/6/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of amendment, remarks, IDS and request for extension of time filed 05/06/04. Examiner also acknowledges receipt of IDS filed 12/05/03. Claims 26-42 are cancelled and claims 1-25 are pending.

Information Disclosure Statement

Examiner acknowledges receipt of the IDS filed 12/05/03 and 05/06/04 and has considered the references cited therein.

1. The indicated allowability of claims 1-25 is withdrawn in view of the newly discovered reference(s) to Miyajima et al (US 4,983,593). Rejections based on the newly cited reference(s) follow. There is also an issue of scope of enablement of concentration enhancing polymer and cholesteryl ester transfer protein. The claims are directed to preparation of a broad composition of cholesteryl ester transfer protein inhibitors and concentration enhancing polymers where the steps are limited broadly dissolution in organic solvent, removing the solvent by evaporation and spray drying that results in atomization.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 6 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for quinoline cholesteryl ester transfer protein inhibitors and carboxymethyl ethyl cellulose and polyoxyethylene-polyoxypropylene block copolymers as the

concentration enhancing polymers, does not reasonably provide enablement for all cholesteryl ester transfer protein inhibitors and all concentration enhancing polymers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Since the state of the art is such that there are concentration enhancing polymers besides the carboxymethyl ethyl cellulose and polyoxyethylene-polyoxypropylene block copolymers disclosed in paragraph [0022] of the specification and since there are other cholesteryl ester transfer protein inhibitors besides the quinolines, the person of skill or of ordinary skill in the art would have to experiment with all the known and yet to be discovered cholesteryl ester transfer protein inhibitors and concentration enhancing polymers to ascertain which of them what combination would work in the instant invention. Because the guidance provided is limited to the quinolines and to carboxymethyl ethyl cellulose and polyoxyethylene-polyoxypropylene block copolymers, it would require tremendous guidance for one to practice the invention.

Regarding the concentration enhancing polymers, the claims may further specify or select those two that are enable by the specification. Similarly, the cholesteryl ester transfer protein inhibitors may further be guided to the disclosed quinolines that are enable in the specification.

Claim Objections

4. Claims 20-24 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 20-24 do not further limit the method steps of preparing

or forming the pharmaceutical composition that contains cholesteryl ester transfer protein inhibitors and concentration enhancing polymers.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-5 and 13-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Miyajima et al. (US 4,983,593).

Miyajima discloses the preparation of pharmaceutical composition that comprises NZ-105 and hydroxypropylmethylcellulose acetate succinate (HPMCAS) (abstract), a concentration-enhancing polymer. NZ-105 inhibits the activity of cholesteryl ester transfer protein (see Kitahara et al and Toyoda et al as teaching references). The preparation process as disclosed by Miyajima involves dissolving NZ-105 and HPMCAS in an organic solvent, removing the solvent by means of vacuum drying, freeze-drying; the NZ-HPMCAS is spray coated (column 3, line 55 to column 4, line 57). It is known that "spray drying is used conventionally and broadly refers to processes involving breaking up liquid mixtures into small droplets (atomization)…droplets" (paragraph [0049] of page 8 of EP 0 901 786, as a teaching reference, which is of similar importance in the instant claims). Molten mixtures generally form when samples are frozen for freeze-drying. The methods recited in claims 20-24 do not limit the method steps in the preparation of pharmaceutical composition but these claims rather recite the properties of the formulation formed by the method and have been examined as claims defining the properties of

the formulation formed by the process; the properties are inherent to the composition and cannot be separated from the composition. Specifically, it is noted that no specific cholesteryl ester transfer protein inhibitors and concentration enhancing polymers are claimed that would otherwise have distinct properties resulting from either the amounts/concentration of the drug-polymer product. Claim 25 is any product formed between the cholesteryl ester transfer protein inhibitors and concentration enhancing polymers. Miyajima meets the limitations of the claims.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 6-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyajima et al. (US 4,983,593) in view of Nakamichi et al. (US 5,456,923).

Miyajima discloses the instant method for forming the pharmaceutical composition. Miyajima does disclose using an extruder. Nakamichi discloses the use of twin-screw extruder to form solid dispersion of mixtures of cardiovascular system drug and concentration enhancing polymers such as hydroxypropylmethylcellulose acetate succinate (HPMCAS or AQOAT) (abstract, column 1, line 54 to column 2, line 59 and claims 1 and 2).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of Miyajima to form pharmaceutical composition of cholesteryl ester transfer protein inhibitors and concentration enhancing polymers. One having ordinary skill in the art would have been motivated to modify the process of Miyajima by

passing the mixture thorough a twin-screw extruder according to the disclosure of Nakamichi with the expectation of heating the mixture below the decomposition temperature of the polymer and the drug during the production of the solid dispersion.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

bf

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